INDICATIONS AND USAGE :
ARTEX (Meloxicam) is indicated for relief of the signs and symptoms of Osteoarthritis, Rheumatoid Arthritis. Ankylosing Spondylitis, Sciatica and Acute Lumbago.

CONTRAINDICATIONS :
ARTEX (Meloxicam) is contraindicated in patients with known hypersensitivity to meloxicam . It should not be given to patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylactic-like reactions to NSAIDs have been reported in such patients.

WARNINGS :
Gastrointestinal ; (GI) Effects - Risk of GI Ulceration, Bleeding and Perforation.
Serious gastrointestinal toxicity, such as inflammation, bleeding , ulceration, and perforation of the stomach, small intestine or large intestine , can occur at any time, with or without warming symptoms, in patients treated with non-steroidal anti-inflammatory drugs (NSAIDs). Minor upper gastrointestinal problems, such as dyspepsia, are common and may also occur at any time during NSAID therapy. Therefore physicians and patients should remain alert for ulceration and bleeding even in the absence of previous GI symptoms. Patients should be informed about the signs and/or symptoms of serious GI toxicity and the steps to take if they occur. It has been domonstrated that upper GI ulcers, gross bleeding or perforation, caused by NSAIDs, appear to occur in approximately 1% of the patients treated for 3-6 month and in about 2-4% of patients treated for one year. These trends continue thus, increasing the likelihood of developing a serious GI event at some time during the course of therapy. However even short-term therapy is not without risk.
NSAIDs should be prescribed with extreme caution in those with a prior history of ulcer disease or gastrointestinal bleeding. Most spontaneous reports of fatal GI events are in elderly or debilitated patients and therefore special care should be taken in treating this population. To minimize the potential risk for an adverse GI event, the lowest effective dose should be used for the shortest possible duration. For high-risk patients alternative therapies that do not involve NSAIDs should be considered.
Hepatic Insufficiency ;
No dose adjustment is necessary in mild to moderate hepatic insufficiency. Patients with severe hepatic impairment have not been adequately studied.
Renal Insufficiency ;
There is no need for dose adjustment in patients with mild to moderate renal failure (CrCL > 15 mL/min). Patients with severe renal insufficiency have not been adequately studied . The use of meloxicam in subjects with severe renal impairment is not recommended.
Pregnancy ;
In late pregnancy, as with other NSAIDs meloxicam should be avoided because it may cause premature closure of the ductus arterlosus.

PRECAUTIONS :
Hepatic Effects ; Borderline elevations of one or more liver tests may occur in up to 15% of patients taking NSAIDs., including meloxicam.
Renal Effects ; Caution should be used when initiating treatment with meloxicam in patients with considerable dehydration. It is advisable to rehydrate patients first and then start therapy with meloxicam. Caution is also recommended in patients with pre-existing kidney disease. Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal medullary changes. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, administration of NSAIDs may cause dose-dependent reduction in prostaglandin formation and secondarily in renal blood flow which may precipitate over renal decompensation. Patients at greatestrisk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and ACE inhibitors and the elderly. Discontinuation of NSAID therapy is usually followed by recovery to the pre-treatment state. The extent to which metabolites may accumulate in patients with renal failure has not been studied with meloxicam. Because some meloxicam metabolites are excreted by the kidney, patierns with significantly impaired renal function should be more closely monitored.
Hematological Effects ;
Anemia is sometimes seen in patients receiving NSAIDs, including meloxicam. This may be due to fluid retention, GI blood loss, or an incompletely described effect upon erythropoiesis. Patients on long-term treatment with NSAIDs, including meloxicam should have their hemoglobin or hematocrit checked if they exhibit any sign or symptoms of anemia.
Fluid Retention And Edema ;
Fluid retention and edema have been observed in some patients taking NSAIDs, including meloxicam. Therefore, as with other NSAIDs, meloxicam should be used with caution in patients with fluid retention, hypertension or heart failure.
Pre-existing Asthma ;
Patients with asthma may have aspirin-sensitive asthma. The use of aspirin in patients with aspirin-sensitive asthma has been associated with severe bronchospasm which can be fatal. Since cross reactivity, including bronchospasm, between aspirin and other nonsteroidal anti-inflammatory drugs has been reported in such aspirin-sensitive patients, meloxicam should not be administered to patients with this form of aspirin sensitivity and should be used with caution in patients with pre-existing asthma.

INFORMATION FOR PATIENTS :
ARTEX (meloxicam) like other drugs of its class, can cause discomfort and, rarely more serious side effects, such as gastrointestinal bleeding which may result in hospitalization and even fatal outcomes. Although serious GI tract ulcerations and bleeding can occur without warning symptoms, patients should be alert for the signs and symptoms of ulcerations and bleeding, and should ask for medical advice when observing any indicative signs or symptoms. Patients should be made aware of the importance of this follow-up.
Patients should report to their physicians signs or symptoms of gastrointestinal ulceration or bleeding, skin rash, weight gain or edema. Patient should be informed of the warning signs and symptoms of hepatoxicity (e.g., nausea, fatigue, lethargy, pruritis, jaundice, right upper quadrant tenderness and "flu like" symptoms). If these occur, patients should be instructed to stop therapy and seek immediate medical therapy. Patient should also be instructed to seek immediate emergency help in the case of any anaphylactoid reaction. In late pregnancy as with other NSAIDs, meloxicam should be avoided because it may cause premature closure of the ductus arteriosus.
Laboratory Tests ;
Patients on long-term treatment with NSAIDs should have their CBC and a chemistry profile checked preodically. If clinical signs and symptoms consistent with liver or renal disease develop systemic manifestations occur (e.g. eosinophilia, rash etc.) or if abnormal liver test persist or worsen, meloxicam should be discontinued.
Drug Interactions ;
ACE Inhibitors
Reports suggest that NSAIDs may diminish the antihypertensive effect of angiotensin-converting enzyme (ACE) inhibitors. This interaction should be given consideration in patients taking NSAIDs concomitantly with ACE inhibitors.
Aspirin
Concomitant administration of Aspirin (1000mg TID) to healthy volunteers tended to increase the AUC (10%) and Cmax (24%) of meloxicam. The clinical significance of this interaction is not known, however, as with other NSAIDs concomitant administration of meloxicam and aspirin is not generally recommended because of the potential for increased adverse effects. Concomitant administration of low-dose aspirin with meloxicam may result in an increased rate of GI ulceration or other complications, compared to use of meloxicam alone. Meloxicam is not a substitute for aspirin for cardiovascular prophylaxis.
Cholestyramine ;
Pretreatment for four days with cholestyramine significantly increased the clearance of meloxicam by 50%. This resulted in a decrease in t1/2, from 19.2 hours to 12.5 hours, and a 35% reduction in AUC. This suggests the existence of a recirculation pathway for melocxicam in the gastrointestinal tract. The clinical relevance of this interaction has not been established.
Cimetidine ;
Concomitant administration of 200mg cimetidine QID did not alter the single-dose pharmacokinetics of 30mg meloxicam.
Digoxin ;
Meloxicam 15mg once daily for 7 days did not alter the plasma concentration profile of digoxin after administration for 7 days at clinical doses. In vitro testing found no protein binding drug interaction between digoxin and meloxicam.
Furosemide ;
Clinical studies as well as post-marketing observations, have shown that NSAIDs can reduce the natriuretic effect of furosemide and thiazide diuretics in some patients. This effect have been attributed to inhibition of renal prostaglandin synthesis. Studies with furosimide agents and meloxicam have not demonstrated a reduction in natriuretic effect. Furosemide single and multiple dose pharmacodynamics and pharmacokinetics are not affected by multiple doses of meloxicam. Nevertheless, during concomitant therapy with furosemide and meloxicam, patient should be observed closely for signs of declining renal function, as well as to assure diuretic efficacy.
Lithium ;
In clinical trials, NSAIDs have produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. Patients on lithium treatment should be closely monitored when meloxicam is introduced or withdrawn.
Methotrexate ;
Meloxicam did not have a significant effect on the pharmacokinetics of single doses of methotrexate. In vitro, methotrexate did not displace meloxicam from its human serum binding sites.
Warfarin ;
Anticoagulant activity should be monitored, particularly in the first few days after initiating or changing meloxicam therapy in patients
receiving warfarin or similar agents, since these patients are at an increased risk of bleeding.
Carcinogenesis, Mutagenesis, Impairment of Fertility ;
No carcinogenic effect of meloxicam was observed in rats at oral doses up to 0.8mg/kg/day. Meloxicam was not mutagenic in an Ames assay.
Meloxicam did not impair male and female fertility in rats at oral doses up to 9 and 5mg/kg/day.
Labor and Delivery ;
Studies in rats with meloxicam, as with other drugs known to inhibit prostaglandin synthesis, showed an increased incidence of stillbirths, increased length of delivery time, and delayed parturition at oral dosages.

Nursing Mothers ;
Studies of meloxicam excretion in human milk have not been conducted; however, meloxicam was excreted in the milk of lactating rats at concentrations higher than those in plasma. Because of the potential for serious adverse reactions in nursing infants from meloxicam, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
Pediatric Use ;
Safety and effectiveness in pediatric patients under 18 years of age have not been established.
Geriatric Use ;
As with any NSAID, caution should be excercised in treating the elderly (65 years and older).

ADVERSE REACTIONS :
The following is a list of adverse drug reactions occuring in <2% of patients receiving Meloxicam in clinical trials involving approximately 15,400 patients.
Body as a whole ; Allergic reaction, anaphylactoid reactions including shock, face adema, fatique, fever, hot fushes, malaise, syncope, weight decrease, weight increase.
Cardiovascular ; Angina pectoris, cardiac failure, hypertension, hypotension, myocardial infarction, vasculitis
Central and Peripheral ; Convulsions, paresthesia, tremor, vertigo.
Nervous System
Gastrointestinal ; Colitis, dry mouth, duodenal ulcer, eructation, esophagitis, gastric ulcer, gastritis, gastroesophageal reflux, gastrointestinal hemorrhage, hematemesis, hemorrhagic duodenal ulcer, hemorrhagic gastric ulcer, intestinal perforation, melena, pancreatitis, perforated duodenal ulcer, perforated gastric ulcer, stomatitis ulcerative.
Heart Rare and Rhythm ; Arrhythmia, palpitation, tachycardia.
Hematologic ; Agranulocytosis, leukopenia, purpura, thrombocytopenia.
Liver and Biliary System ; ALT increased, AST increased, bilirubimenia, GGT increased, hepatitis, jaundice, liver failure.
Metabolic and Nutritional ; Dehydration.
Psychiatric Disorders ; Abnormal dreaming, anxiety, appetite increased, confusion, depression.
Nervousness,somnolence
Respiratory ; Asthma, bronchospasm, dyspnea.
Skin And Appendages ; Alopecia, angioedema, bullous eruption, erythema multiforme, photosensitivity reaction, pruritus, Stevens Johnson syndrome, sweating increased, toxic epidermal necrolysis, urticaria.
Special Senses ; Abnormal vision, conjunctivitis, taste perversion, tinnitus.
Urinary System ; Albuminuria, BUN increased, creatinine increased, hematuria, interstitial nephritis, renal failure.

OVERDOSAGE :
There is limited experience with meloxicam overdose. Four cases have taken 6 to 11 times the highest recommended dose: all recovered. Cholestyramine is known to accelerate the clearance of meloxicam. Symptoms following acute NSAID overdose are usually limited to lethargy, drowsiness, nausea, vomiting and epigastric pain, which are generally reversible with supportive care. Gastrointestinal bleeding can occur. Severe poisoning may result in hypertension,\ acute renal failure, hepatic dysfunction, respiratory depression, coma, vonvulsions, cardio-vascular collapse and cardiac arrest Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following an overdose. Patients should be managed with symptomatic and supportive care following an NSAID overdose. In cases of acute overdose, gastric lavage followed by activated charcoal is recommended. Gastric lavage performed more than one hour after overdose has little benefit in the treatment of overdose. Administration of activated charcoal is recommended for patients who present 1-2 hours after overdose. For substantial overdose or severely symptomatic patients, activated charcoal may be administered repeatedly. Accelerated removal of meloxicam by 4 gm oral doses of cholestyramine given three times a day was demonstrated in a clinical trial. Administration of choloeslyramine may be useful following and overdose Forced diuresis, alkalinization of urine, hemodialysis or hemoperfusion may not be useful due to high protein binding.

DOSAGE AND ADMINISTRATION:
The lowest dose of ARTEX (meloxicam) should be sought for each patient. The recommended starting and maintenance dose of ARTEX is 7.5 mg once daily. Some patients may receive additional benefit by increasing the dose to 15 mg once daily. The maximum recommended dose of ARTEX is 15 mg. once daily or as recommended by the physician. ARTEX may be taken without regard to timing of meals.

AVAILABILITY :

ARTEX - 7.5mg Tablet	Each film coated tablet contains meloxicam 7.5mg. Pack of 10's in blister.
ARTEX - 15mg Tablet	Each film coated tablet contains meloxicam 15mg. Pack of 10's in blister.

STORAGE:
Store in a cool and dry place. Keep away from direct sunlight and out of the reach of children.

Revised : Aug. 2016

دھوپ سے گرمی اور نمی سے محفوظ رکھیں ۔
تمام ادویات بچوں کی پہنچ سے دور رکھیں ۔
ڈاکٹری ہدایات کے مطابق استعمال کریں ۔

Manufactured by:
PHARMEDIC LABORATORIES (PVT) LIMITED
16 Km. Multan Road, Lahore - Pakistan

ARTEX
(MELOXICAM)
7.5mg, 15mg Tablets

آرٹیکس 7.5 ملی گرام - 15 ملی گرام
ٹیبلیٹس
(میلوکسی کیم)

DESCRIPTION :
ARTEX (meloxicam), an oxicam derivative, is a member of the enolic acid group of nonsteroidal anti-inflammatory drugs (NSAIDs).
Each tablet contains meloxicam 7.5 or 15 mg for oral administration.

CLINICAL PHARMACOLOGY :
Mechanism of Action ;
Meloxicam is a nonsteroidal anti-inflammatory drug (NSAID) that exhibitis anti-inflammatory, analgesic and anti-pyretic activities in animal models. The mechanism of action of meloxicam, like that of other NSAIDs., may be related to prostaglandin synthetase (cyclooxygenase) inhibition.

PHARMACOKINETICS :
Absorption ;
The absolute bioavailability of meloxicam capsules was 89% following a single oral dose of 30 mg compared with 30 mg IV bolus injection. Meloxicam capsules have been shown to be bioequivalent to meloxicam tablets. Following single intravenous dose, dose-proportional pharmacokinetics were shown in the range of 5 mg to 60 mg. After multiple oral doses the pharmacokinetics of meloxicam capsules were dose-proportional over the range of 7.5 mg to 15 mg. Mean Cmax was achieved within four to five hours after a 7.5 mg meloxicam tablet. The rate or extent of absorption was not affected by multiple dose administration, suggesting linear pharmacokinetics. With multiple dosing, steady state condition were reached by day 5. A second meloxicam concentration peak occurs around 12 to 14 hours post-dose suggesting gastrointestinal recirculation.
Food and Antacid Effects ;
ARTEX (meloxicam) tablets can be administered without regard to timing of meals and antacids.
Distribution ;
The mean volume of distribution (Vss) of meloxicam is approximately 10 L. Meloxicam is 99.4% bound to human plasma proteins (primarily albumin) within the therapeutic dose range. The fraction of protein binding is independent of drug concentration, over the clinically relevant concentration range, but decreases to 99% in patients with renal disease. Meloxicam penetration into human red blood cells, after oral dosing is less than 10% . Following a radiolabeled dose, over 90% of the radioactivity defected in the plasma was present as unchanged meloxicam. Meloxicam concentrations in synovial fluid, after a single oral dose, range from 40% to 50% of those in plasma. The free fraction in synovial fluid is 2.5 times higher than in plasma, due to the lower albumin content in synovial fluid as compared to plasma. The significance of this penetration is unknown.
Metabolism ;
Meloxicam is almost completely metabolized to four pharmacologically inactive metablites. The major metabolite. 5-carboxy meloxicam (60% of dose), from P-450 mediated metabolism was formed by oxidation of an intermediate metabolite 5-hydroxymethyl meloxicam which is also excreted to a lesser extent (9% of dose). In vitro studies indicate that cytochrome P-450 2C9 plays an important role in this metabolic pathway with a minor contribution of the CYP 3A4 isozyme. Patients peroxidase activity is probably responsible for the other two metabolites which account for 16% and 4% of the administered dose respectively.
Excretion ;
Meloxicam excretion is predominantly in the form of metabolites and occurs to equal extents in the urine and feces. Only traces of the unchanged parent compound are excreted in the urine (0.2%) and feces (1.6%). The extent of the urinary excretion was confirmed for unlabeled multiple 7.5 mg doses: 0.5%, 6% and 13% of the dose were found in urine in the form of meloxicam and the 5-hydroxymethyl and 5" - carboxy metabolites, respectively. there is significant biliary and/or enteral secretion of the drug. This was demonstrated when oral administration of cholestyramine following a single IV dose of meloxicam decreased the AUC of meloxicam by 50%. The mean elimination half-life (t1/2) ranges from 15 hours to 20 hours . The elimination half-life is constant across dose levels indicating linear metabolism within the therapeutic dose range. Plasma clearance ranges from 7 to 9 mL/min.

SPECIAL POPULATION :
Pediatric ;
The pharmacokinetics of Meloxicam in pediatric patients under 18 years of age have not been investigated.
Geriatric ;
Elderly males (65 years of age) exhibited meloxicam plasma concentrations and steady state pharmacokinetics similar to young males. Elderly females (65 years of age) had a 47% higher AUCss and 32% higher Cmax ss as compared to younger females (55 years of age) after body weight normalization. Despite the increased total concentrations in the elderly females, the adverse event profile was comparable for both elderly patient populations. A smaller free fraction was found in elderly female patients in comparison to elderly male patients.
Gender ;
Young females exhibited slightly lower plasma concentrations relative to young males. After single dose of 7.5 mg meloxicam, the mean elimination half-life was 19.5 hours for the female group as compared to 23.4 hours for the male group. At steady state the data were similar (17.9 hours vs 21.4 hours). This pharmacoknetic difference due to gender is likely to be of little clinical importance. There was linearity of pharmacokinetics and no appreciable difference in the Cmax or Tmax across genders.